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Genentech Patent Docket P1819R1

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of  
David G. Lowe et al.  
Serial No.: 09/823,648

Filed: 30 March 2001

For: COMPOSITIONS AND METHODS  
FOR DETECTING AND  
QUANTIFYING GENE  
EXPRESSION

Group Art Unit: 1655

Examiner: A. Chakrabarti

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## CERTIFICATE UNDER 37 CFR 1.10

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July 19, 2002

Yvonne Carter

Response to Non Final Office Action Under 37 C.F.R. § 1.111

Assistant Commissioner of Patents  
Washington, D.C. 20231

Sir:

This document is responsive to the Office Action mailed January 30, 2002 (Paper No. 12) for which a three month period for response was given. This document is timely filed with a Three Month Petition to Extend Time to include 30 July 2002. In view of the discussion provided, reconsideration and allowance are respectfully requested.

In the Claims:

Please cancel claims 41-104 without prejudice to later prosecution, leaving claims 1-40 pending in the application.

Please amend claims 4, 17, and 25 to read as follows:

A1  
4. The microarray of claim 3, wherein the polynucleotide is selected from the group consisting of an oligonucleotide, DNA, amplified DNA, cDNA, single stranded DNA, double stranded DNA, PNA, RNA, and mRNA.

A2  
17. The microarray of claim 15, wherein the substrate is in a form selected from the group consisting of threads, sheets, films, gels, membranes, beads, and plates.

A3  
25. A microarray prepared by a method comprising:  
(a) providing a multifunctional linker reagent comprising two or more reactive groups, wherein a first reactive group reacts with a functional group of a microarray substrate and a second reactive group reacts with a target molecule;  
(b) activating the substrate surface for immobilizing the target molecule, by silanizing the surface with a silane in toluene in the absence of acetone or an alcohol, wherein the silane comprises a functionality reactive with the multifunctional linker reagent, and wherein the activating further comprises immobilizing the multifunctional linker reagent on the silanized surface by attaching the multifunctional linker reagent to the silane via the first reactive group of the linker reagent and a reactive group of the silane;  
(c) providing a solution comprising a target molecule having one or more functional groups reactive with the second reactive group of the immobilized multifunctional linker reagent;  
(d) attaching the target molecule to the substrate surface by contacting the target molecule with the activated substrate surface under conditions that promote attachment of the target molecule to the immobilized multifunctional linker reagent.

REMARKS

Formal Matters

Claims 1-40 are pending in the application. Claims 41-104 are canceled, without prejudice to later prosecution, in response to the restriction requirement mailed December 5, 2001, although Applicant respectfully maintains traversal of the requirement.

Claims 4, 17, and 25 are amended.

Amendment to claim 4 is made merely to correct an inadvertent typographical error. Claim 17 is amended to delete the phrase "and like" and to generate a Markush group.

Claim 25 is amended to delete the phrase "capable of" and distinctly point out reactivities of a first and a second reactive group of the multifunctional linker reagent. Support for the amendment is found throughout the specification, such as, for example, at page 3, lines 32-34; page 4, lines 4-10; page 5, lines 32-36; page 7, lines 1-6 and lines 17-28; page 10, line 33 to page 11, line 6; page 14, lines 21-28; page 16, lines 7-10; and page 33, lines 1-2.

No new matter is added by the amendments.

Rejection Under 35 U.S.C. §112, Second Paragraph

Claims 17 and 25-40 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. According to the rejection, the phrase "and like" in claim 17 allegedly renders the scope of the claim unascertainable, and the phrase "capable of" in claim 25 allegedly renders limitations following the phrase unclear. Applicants respectfully traverse the rejections as applied and as they might be applied to the currently pending claims for the reasons provided below.

Without acquiescing to the rejection and merely to expedite prosecution and allowance of the pending claims, Applicants have amended claim 17 to delete the phrase "and like" and to provide the substrate forms in a Markush group. Applicants respectfully submit that the rejection has been overcome. Allowance of claim 17 is respectfully requested.

Claim 25 is amended to delete the phrase "capable of" merely to expedite prosecution and allowance of the pending claims and without acquiescing to the rejection. In traversing the rejection, Applicants respectfully point out that one of ordinary skill in the art would recognize that a claim reciting a reactive group "capable of" a particular limitation necessarily includes that limitation, thereby rendering the claim definite under Section 112, second paragraph. Without acquiescing to the rejection, Applicants recite a multifunctional linker reagent comprising two or more reactive groups, wherein a first reactive group reacts with a functional group of a microarray substrate and a second reactive group reacts with a target molecule. Support for the amendment is provided throughout the originally filed specification as listed herein, above. No new matter is added by the amendment. Claim 25, and claims 26-40 depending from it, are in condition for allowance, which action is respectfully requested.

Rejection Under 35 U.S.C. § 102(a) (Thompson et al.)

Claims 1-9, 15-19, 25-27, and 40 were rejected under 35 U.S.C. § 102(a) as allegedly anticipated by Thompson et al. (WO 99/20640, published April 29, 1999). Applicants respectfully traverse the rejection as applied and as it might be applied to the currently pending claims for the reasons provided below.

The Examiner states at page 3, item 5 of the Office Action that Thompson et al. teach a microarray comprising a surface silanized with a silane in toluene in the absence of acetone or an alcohol. Applicants respectfully disagree and point out that at none of the citations listed by the Examiner (on pages 3 or 4 of the Office action) does the Thompson et al. reference contemplate, suggest, or disclose silanizing in toluene in the absence of acetone or an alcohol. A cited reference does not anticipate a claim unless each and every limitation of the claim is recited in the cited reference. (See *In re Donohue*, 226 USPQ 619, 621 (Fed. Cir. 1985) (discussing anticipation under § 102(b)), as applicable to the present § 102(a) rejection). Lacking the Applicants' limitation of silanizing in toluene in the absence of acetone or an alcohol, Thompson et al. does not anticipate the

claims. As a result, the rejection is improper and should be withdrawn, which action is respectfully requested.

Rejection Under 35 U.S.C. § 103(a) (Thompson et al.)

Claims 1-9, 15-19, 25-27, and 30-40 were rejected under 35 U.S.C. § 103(a) over Thompson et al., *supra*. Applicants respectfully traverse the rejection as applied and as it might be applied to the currently pending claims for the reasons provided below.

Contrary to the Examiner's assertion, Thompson et al. does not teach a microarray of Applicants' claims 1-9, 15-19, 25-27 and 40 as Applicants have discussed, above, because Thompson et al. does not suggest or disclose silanizing in toluene in the absence of acetone or an alcohol. By failing to even suggest this limitation of Applicants' claims, Thompson et al. does not render Applicants claims obvious. One of ordinary skill in the relevant art would consider silanizing in toluene in the absence of acetone or an alcohol because such is not contemplated or suggested by the Thompson et al. reference.

Applicants' disclosure of polynucleotide concentration on a spot, the pH range of the attaching step, or the time range for attachment do not render the claims *prima facie* obvious whether or not such limitations are routinely derived. Applicants' claimed invention is not obvious, much less *prima facie* obvious, in view of Thompson et al. because Thompson et al. does not contemplate or suggest silanizing in toluene in the absence of acetone or an alcohol. As a result, the rejection is improper and should be withdrawn, which action is respectfully requested.

Rejection Under 35 U.S.C. § 103(a) (Thompson et al., Dintzis et al.)

Claims 1-19 and 25-40 were rejected under 35 U.S.C. § 103(a) over Thompson et al., *supra*, in view of Dintzis et al. (US 6,340,460 B1, issued January 22, 2002). Applicants respectfully traverse the rejection as applied and as it might be applied to the currently pending claims for the reasons provided below.

Contrary to the Examiner's assertion, Thompson et al. does not teach a microarray of Applicants' claims 1-9, 15-19, 25-27 and 30-40 as Applicants have discussed, above, because Thompson et al. does not contemplate or suggest silanizing in toluene in the absence of acetone or an alcohol.

The Dintzis et al. reference does not cure the deficiency of Thompson et al. Dintzis et al. disclose a method of preparing a non-immunogenic construct for reducing a non-primary antibody response to an epitope of a T-dependent antigen by coupling two or more copies of the epitope to a non-immunogenic soluble carrier (see Abstract). The authors also disclose incorporating a primary amino group into a polynucleic acid (see col. 37, lines 48-50). Dintzis et al. does not cure the deficiency of Thompson et al. because, not only is the field of the Dintzis et al. reference outside that of microarrays, but the Dintzis et al. disclosure does not contemplate or suggest silanizing a substrate in toluene in the absence of acetone or an alcohol.

The combination of Thompson et al. and Dintzis et al. fails to contemplate or suggest Applicants' claimed invention. As a result, Applicants' claimed invention is not rendered obvious in view of the references in combination. Further, the Examiner has failed to support a *prima facie* obviousness rejection because (1) the fields of the references differ such that one of ordinary skill in the art would not be motivated to combine them, and (2) the combination does not cure the deficiency of either cited reference thereby giving the ordinarily skilled artisan no motivation to combine the cited references. Thus, the rejection is improper and should be withdrawn, which action is respectfully requested.

Rejection Under 35 U.S.C. § 103(a) (Thompson et al., Friend et al.)

Claims 1-9, 15-21, 25-27, and 30-40 were rejected under 35 U.S.C. § 103(a) over Thompson et al., *supra*, in view of Friend et al. (US 6,324,479 B1, issued November 27, 2001). Applicants respectfully traverse the rejection as applied and as it might be applied to the currently pending claims for the reasons provided below.

Contrary to the Examiner's assertion, Thompson et al. does not teach a microarray of Applicants' claims 1-9, 15-19, 25-27 and 30-40 as Applicants have discussed, above, because Thompson et al. does not contemplate or suggest silanizing in toluene in the absence of acetone or an alcohol. Applicants agree, however, that Thompson et al. does not teach attaching a target molecule to a surface by printing or deposition on a mask.

Friend et al. discloses methods for determining the level of protein activity under various circumstances involving target molecules. In some cases, the target molecule, such as a nucleic acid, is attached to a solid surface in a microarray, which attachment may be accomplished by, for example, photolithography or printing (see col. 34, lines 28-56). The Friend et al. reference does not contemplate or suggest silanizing a surface in toluene in the absence of acetone or an alcohol.

Combining the Thompson et al. and Friend et al. references does not cure the deficiency of either reference. Because neither reference contemplates or suggests a limitation of Applicants' claimed invention (silanization in toluene in the absence of acetone or an alcohol), there is no motivation for one of ordinary skill in the art to combine them to achieve Applicants' invention. Even if the references were combined (although there is no motivation to do so), the combination fails to yield Applicants' claimed invention. The printing limitation discussed by the Examiner at page 10 of the Office Action fails to make a showing of *prima facie* obviousness because it fails to contemplate a limitation of Applicants claimed invention. As a result, the rejection is improper and should be withdrawn, which action is respectfully requested.

Rejection Under 35 U.S.C. § 103(a) Thompson et al., Dintzis et al., Friend et al.)

Claims 1-19 and 22-40 were rejected under 35 U.S.C. § 103(a) over Thompson et al., *supra*, in view of Dintzis et al., *supra*, and further in view of Friend et al., *supra*. Applicants respectfully traverse the rejection as applied and as it might be applied to the currently pending claims for the reasons provided below.

For the reasons discuss above, Applicants point out that none of the cited references, Thompson et al., Dintzis et al., and Friend et al., contemplate, suggest, or disclose a microarray comprising a surface silanized with a silane in toluene in the absence of acetone or an alcohol. Despite the teachings of each of the references as discussed in the Office Action at pages 10 and 11, there is no motivation to combine the references because the deficiency of each (the lack of any suggestion of silanizing in toluene in the absence of acetone or an alcohol) fails to cure the deficiency of any one or two of the other references. There is no motivation to combine the references and the combination, if made, is deficient. As a result, the Examiner has made no showing of *prima facie* obviousness, or any form of obviousness, of Applicants' claims in view of the cited references. The rejection is improper and should be withdrawn, which action is respectfully requested.

#### SUMMARY

Claims 1-40 are pending in the application. Claims 41-104 are canceled without prejudice to later prosecution. Claims 4, 17, and 25 are amended. No new matter is added by the amendments.

The rejections under Section 112, second paragraph are overcome, although the amendments to the claims are made merely to expedite prosecution and allowance of the claims and without acquiescing to the Examiner's rejection.

The rejections under Section 102(a) in view of Thompson et al. and the rejections under Section 103(a) over Thompson et al. in view of either Dintzis et al. and/or Friend et al. are overcome by pointing out that none of the references suggest or disclose a limitation of Applicants' claimed invention, nor does any combination of the references cure the deficiencies of others.

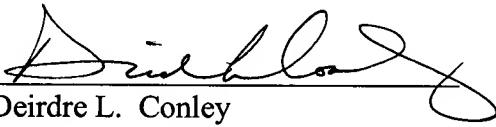
The pending claims are in condition for allowance, which action is respectfully requested.

If in the opinion of the Examiner, a **telephone conference** would expedite the prosecution of the subject application, the Examiner is **strongly encouraged** to call the undersigned at the

number indicated below.

This response/amendment is submitted with a transmittal letter and petition for a three-month extension of time. In the unlikely event that this document is separated from the transmittal letter, Applicants petition the Commissioner to authorize charging our Deposit Account 07-0630 for any fees required or credits due and any extensions of time necessary to maintain the pendency of this application.

Respectfully submitted,  
GENENTECH, INC.

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